Summary

The following β-mercaptoketones were prepared : 1-Phenyl-3-mercapto-3-(2-thienyl)-, 1-(2-thienyl)-3-mercapto-3-phenyl-, 1,3-di-2-thienyl-3-mercapto-, 1-phenyl-3-mercapto-3-(2-furyl)-, and 1-(2-furyl)-3-mercapto-3-phenyl-1-propanone were prepared by the addition of hydrogen sulfide to the corresponding α,β-unsaturated ketones. These mercaptoketones formed chelate compounds with copper and the ratio of ligand to copper was found to be 1:1.

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169. **Hisashi Tanaka and Akira Yokoyama** : Studies on the Sulfur-containing Chelating Agents. IV.[*1] Structure of Copper Chelate of β-Mercaptoketones.

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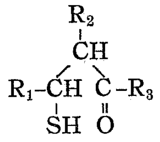
In the previous papers,[1,2][*1] it was reported that β-mercaptoketones, represented by the general formula (A), formed a stable copper chelates.



$$\mathrm{R_1{-}\underset{\displaystyle SH}{CH}{-}\overset{\displaystyle R_2}{CH}{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}R_3}$$

(A)

$R_1 = R_3 =$ aryl

$R_2 =$ H, alkyl, or aryl

This paper deals with the structure of these copper chelates. The ratio of ligand to copper was expected to be one to one or two to one, and, from the result of microanalysis, the ratio was found to be one to one.

In the course of preparation of the copper chelate, after the copper chelate was separated, colorless crystals appeared from the residual solution. In the case of $R_1=R_3=$phenyl, $R_2=$H, namely, 3-mercapto-3-phenylpropiophenone, colorless needles which melted at 156° were obtained. This substance was identified with the corresponding disulfide, reported in Part I.[1] Moreover, when 3-mercapto-3-phenylpropiophenone was oxidized with hydrogen peroxide, the same substance was also obtained. Molecular weight was measured and the value found agreed with the calculated value for the disulfide. Accordingly, formation of a disulfide with the chelate formation was confirmed.

As a result of above-mentioned experiments, formation of copper chelate was considered to proceed according to Chart 1, namely, Cu^{2+} was reduced to Cu^{+} by the mercaptoketone and the mercaptoketone was oxidized to disulfide simultaneously, Cu^{+} forming a chelate with the mercaptoketone.[3] About 1/2 mole of copper chelate was obtained from 1 mole of mercaptoketone, as shown in Table III in the Experimental part. In

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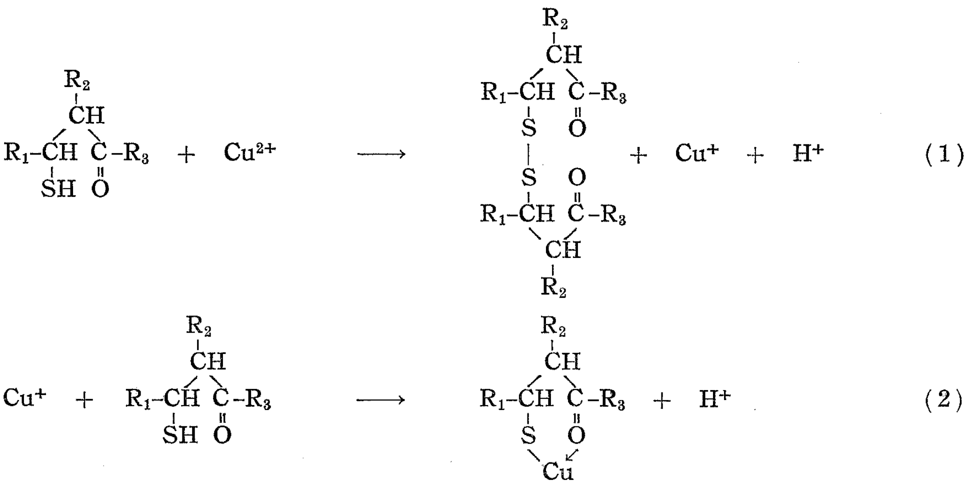
[*1] Part III : This Bulletin, 8, 1008(1960).

[*2] Sakyo-ku, Kyoto (田中 久, 横山 陽).

1) Part I : This Bulletin, 8, 275(1960).

2) Part II : *Ibid.*, 8, 280(1960).

3) H. Tanaka, A. Yokoyama : Paper read at the 12th Annual Meeting of the Pharmaceutical Society of Japan, April, 1959.



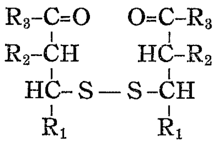
from (1) and (2)

$$2R\text{-}SH + Cu^{2+} \longrightarrow RSCu(\text{I}) + \tfrac{1}{2}R\text{-}S\text{-}S\text{-}R + 2H^{+}$$

Chart 1. Formation of Copper Chelate

addition, copper-chelate prepared from Cu^{2+} was found to be identical with the chelate prepared from Cu^{+}. Similar experiments were carried out with other mercaptoketones and the corresponding disulfides listed in Table I were obtained. In the case of 3-mercapto-3-phenyl-4′-chloropropiophenone, chlorine was removed by copper[2] and the chelate which did not contain chlorine was obtained. However, bis(1-phenyl-3-*p*-chlorophenyl-3-oxopropyl) disulfide was obtained at the same time.

TABLE I. Disulfide



R_1	R_2	R_3	m.p. (°C)	mol. wt.	
				Calcd.	Found
Phenyl	H	Phenyl	155	482	477
p-Chlorophenyl	〃	〃	197	551	542
Phenyl	〃	*p*-Chlorophenyl	160	551	536
〃	〃	*p*-Methoxyphenyl	168	542	529
〃	Methyl	Phenyl	89～90	—	—
2-Furyl	H	〃	150	—	—

Infrared spectra of the mercaptoketones, disulfides, and copper chelates were measured to compare each other. In the case of mercaptoketones, absorptions were observed at 2580 and 1680 cm^{-1}, based on the mercapto and keto group, respectively. On the contrary, in the case of disulfides and copper chelates, the absorption at 2580 cm^{-1} was not observed.

Judging from the above-mentioned experimental results, the copper chelates of these mercaptoketones were found to be the chelates of copper(I), with a structure shown in Chart 1. The reaction between copper and thiol, similar to that shown in Chart 2, was reported recently only in the case of mercaptoacetic acid[4] and mercaptosuccinic acid.[5]

Absorption spectra of 3-mercapto-3-(*p*-methoxyphenyl)propiophenone, 3-mercapto-3-(2-furyl)propiophenone, and 1-(2-thienyl)-3-mercapto-3-phenyl-1-propanone, and their

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4) S.B. Sant: Anal. Chem., **31**, 1879(1959).
5) I.M. Klotz, G.H. Czerlinski: J. Am. Chem. Soc., **80**, 2920(1958).

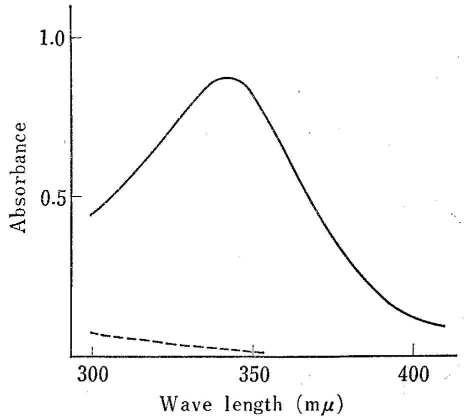


Fig. 1. Absorption Spectra of 3-Mercapto-3-(p-methoxyphenyl)propiophenone (dotted line, concn., $1\times10^{-4}M$ in $CHCl_3$) and its Copper Chelate (solid line, concn., $1\times10^{-4}M$ in $CHCl_3$)

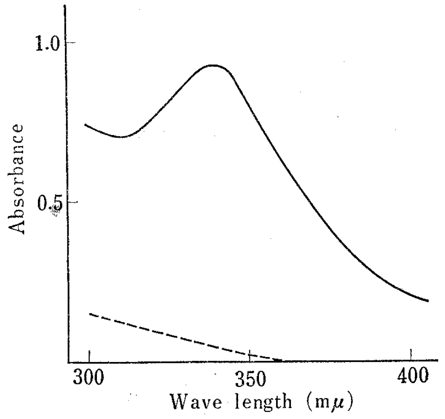


Fig. 2. Absorption Spectra of 3-Mercapto-3-(2-furyl)propiophenone (dotted line, concn., $1\times10^{-4}M$ in $CHCl_3$) and its Copper Chelate (solid line, concn., $1\times10^{-4}M$ in $CHCl_3$)

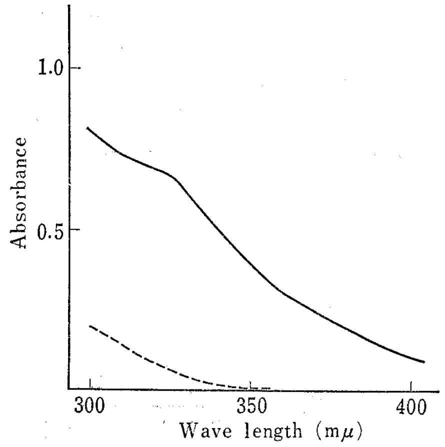
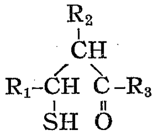


Fig. 3. Absorption Spectra of 1-(2-Thienyl)-3-mercapto-3-phenyl-1-propanone (dotted line, concn., $1\times10^{-4}M$ in $CHCl_3$) and its Copper Chelate (solid line, concn., $1\times10^{-4}M$ in $CHCl_3$)

copper chelates are shown in Figs. 1, 2, and 3, respectively. No remarkable absorption maximum was found in the visible region, but, in the ultraviolet region, a maximum was observed at about 330~340 mμ in every case.

In order to investigate sensitivity of this chelate formation, recognizable limits of copper ion with these mercaptoketones were measured, using the aqueous solution of

TABLE II. Recognizable Limit of Copper by β-Mercaptoketone

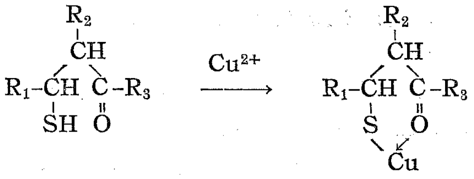


$$R_1\text{-}\underset{SH}{CH}\text{-}\overset{R_2}{CH}\text{-}\underset{O}{\overset{\|}{C}}\text{-}R_3$$

R_1	R_2	R_3	Recognizable limit (γ/0.05 cc.)
Phenyl	H	Phenyl	2.5
m-Tolyl	〃	〃	2.5
p-Methoxyphenyl	〃	〃	4.0
1-Naphthyl	〃	〃	4.0
2-Thienyl	〃	〃	5.0
2-Furyl	〃	〃	2.5
Phenyl	Methyl	〃	5.0
〃	Phenyl	〃	10.0
〃	H	p-Methoxyphenyl	3.0
〃	〃	2-Thienyl	5.0

copper acetate and 1% ethanolic solution of mercaptoketones. The same values were obtained in the case of Cu^{2+} and Cu^{+} prepared by reduction of Cu^{2+} with sodium hydrogensulfite. However, these mercaptoketones were not so sensitive to copper as shown in Table II and no marked difference was found among the mercaptoketones with various substituents.

Table III. Yield of Copper Chelate from Thiol



R_1	R_2	R_3	Thiol taken		Cu added	Chelate obtained	
			(mg.)	(mole × 10^{-3})	(mg.)	(mg.)	(mole × 10^{-3})
Phenyl	H	Phenyl	240	1	50	140	0.46
p-Chlorophenyl	〃	〃	140	0.5	30	80	0.24
Phenyl	〃	*p*-Chlorophenyl	140	0.5	30	70	0.23
〃	〃	*p*-Methoxyphenyl	140	0.5	30	80	0.24
〃	Methyl	Phenyl	250	1	50	140	0.44
2-Furyl	H	〃	230	1	40	140	0.48

Experimental

Preparation of Copper Chelates and Isolation of Disulfides—EtOH solution of thiol and aqueous solution of Cu^{2+} were mixed and warmed on a water bath with shaking for a few min. An orange-red viscous oily precipitate (Cu chelate) separated out. The solvent was decanted and evaporated. Crystals of disulfide obtained were purified as described in the previous papers.1,2),*1 The crude Cu chelate solidified while standing in the air and was recrystallized from EtOH-$CHCl_3$. Yields of Cu chelates are shown in Table III.

Oxidation of 3-Mercapto-3-phenylpropiophenone to Bis(1,3-diphenyl-3-oxopropyl) Disulfide with H_2O_2—To a solution of 3-mercapto-3-phenylpropiophenone (1 g.) in EtOH (150 cc.), 10% H_2O_2 (30 cc.) was added dropwise with stirring at room temperature and stirring was continued for 5 hr. After removing the solvent, disulfide obtained was recrystallized from $CHCl_3$ to colorless needles, m.p. 156.5°. Yield, 0.9 g. The mixed m.p. with bis(1,3-diphenyl-3-oxopropyl) disulfide, reported in Part I,1) did not show any depression.

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Summary

The structure of copper chelates and the mechanism of chelate formation of β-mercaptoketones were investigated and confirmed to be as follows : β-Mercaptoketones reduce Cu^{2+} to Cu^{+} and form chelate with Cu^{+} in the ratio of one to one. At the same time mercaptoketones are oxidized to disulfides.

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